

B2 transesterification products of vegetable oils (such as soybean oil, almond oil, sunflower oil, olive oil or corn oil) with glycerol and perflubron.

IN THE CLAIMS:

Replace the indicated claims with:

B2
Sub C2
16. (Amended) A composition comprising stable solid particles of a water-insoluble biologically active substance of a volume weighted mean particle size in the range of 0.01 to 10 micrometers, which particles are dispersed in a non-aqueous carrier system comprised of:
a non-aqueous hydrophobic liquid in which said biologically active substance is not soluble or is poorly soluble;
a surfactant system consisting of at least one surfactant which is soluble in said non-aqueous hydrophobic liquid, wherein at least a portion of which surfactant system adsorbs to the surface of said particles; and
a quantity of not more than about 10% of the total weight of said composition of one or more hydrophilic substances that provides a self-dispersing property to said composition, wherein upon addition of said composition to a fluid aqueous medium, said composition self-disperses in said fluid aqueous medium to form a suspension comprising droplets of non aqueous hydrophobic liquid containing particles of surface stabilized water-insoluble biological substance suspended in the oily droplets of the dispersion and particles of said water-insoluble biologically active substance migrated into said fluid aqueous medium wherein said particles have a size in the range of 0.01 to 10 micrometers and have associated therewith on the surface at least a portion of said surfactant system.

SUB D1
17. (Amended) The composition of claim 16 where at least one component of the non-aqueous hydrophobic liquid is selected from the group consisting of an oil derived from animal origin; a vegetable oil; a fish oil; a fish oil free fatty acid; oleic acid; linoleic acid; a polyunsaturated fatty acid; caprylic/capric triglyceride; caprylic/capric/linoleic triglyceride; a synthetic medium chain triglyceride having a C₈₋₁₂ fatty acid chain; propylene glycol dicaprylate/caprate; linoleic acid ethyl ester; a cholesteryl fatty acid ester, a C₁₂₋₁₈ fatty acid monoglyceride, a C₁₂₋₁₈ fatty acid diglyceride, and a C₁₂₋₁₈ fatty acid triglyceride prepared from soybean oil, almond oil, sunflower oil, olive oil, and corn oil with glycerol; a pharmaceutically acceptable monohydric alcohol; a pharmaceutically acceptable alkanol; a pharmaceutically acceptable dihydric alcohol; a pharmaceutically acceptable aromatic ester; benzyl benzoate; diethyl phthalate; propyl gallate; triacetin; diacetin; monoacetin; triethyl

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citrate; a pharmaceutically suitable hydrophobic organic solvent; a hydrofluorocarbon in the liquid state at ambient temperature and pressure; and perflubron.

18. (Amended) The composition of claim 16 where at least one surfactant component is selected from the group consisting of a natural or synthetic amphiphilic agent; a phospholipid; a nonionic surfactant; a polyoxyethylene fatty alcohol ether; a sorbitan fatty acid ester; a polyoxyethylene sorbitan fatty acid ester; glycerol triacetate; a polyethylene glycol; cetyl alcohol; cetostearyl alcohol; stearyl alcohol; a poloxamer; a polaxamine; a polyoxethylene castor oil derivative; vitamin E; D-alpha-tocopheryl polyethylene glycol 1000 succinate; vitamin E TPGS; a PEG glyceryl fatty acid ester; PEG-8 glyceryl caprylate/caprate; PEG-4 glyceryl caprylate/caprate; PEG-32 glyceryl laurate; PEG-6 glyceryl mono oleate; PEG-6 glyceryl linoleate; a propylene glycol mono fatty acid ester; a propylene glycol di-fatty acid ester; propylene glycol laurate; propylene glycol caprylate/caprate; diethylene glycol monoethyl ether; transcuto; a monoglyceride; an acetylated monoglyceride; glycerol monooleate; glycerol monostearate; a mono-acetylated monoglyceride; a di-acetylated monoglyceride; monoacetin; diacetin; an anionic surfactant; a fatty acid salt; a bile salt; potassium laurate; triethanolamine stearate; sodium lauryl sulfate; an alkyl polyoxyethylene sulfate; sodium alginate; dioctyl sodium sulfosuccinate; sodium carboxymethylcellulose; calcium carboxymethylcellulose; a cationic surfactant; a pharmaceutically acceptable quaternary ammonium compound; benzalkonium chloride; cetyltrimethylammonium bromide; lauryldimethylbenzylammonium chloride; polyethylene glycol; PEG 1000; PEG 1500; and PEG 3400.

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Sub C3
23. (Amended) The composition of claim 16, wherein the biologically active substance is selected from the group consisting of nifedipine, ursodiol, budesonide, peclitaxel, camptothecin, a derivative of peclitaxel, a derivative of camptothecin, piroxicam, itraconazole, acyclovir, a derivative of acyclovir, fenofibrate, cyclosporine, and insulin.

SUB D1
24. (Amended) The composition of claim 16 which is prepared for sustained or controlled delivery of the biologically active substance.

25. (Amended) The composition of claim 16 where the fluid aqueous medium is selected from the group consisting of water, buffered water, phosphate buffered water, phosphate buffered saline, citrate buffered water, acetate buffered water, water buffered with pharmaceutically acceptable pH controlling agents, water containing salts, water containing sodium chloride, water containing pharmaceutically acceptable salts, water containing soluble

B3 agents for lyoprotection, water containing soluble agents for cryoprotection, water containing dextrose, water containing mannitol, water containing trehalose, water containing sucrose, water containing sorbitol, water containing polyhydroxy-containing compounds, and a mixture thereof.

B4 31. (Amended) The process of claim 30 where at least one component of the non-aqueous hydrophobic liquid is selected from the group consisting of an oil derived from animal origin; a vegetable oil; a fish oil; a fish oil free fatty acid; oleic acid; linoleic acid; a polyunsaturated fatty acid; caprylic/capric triglyceride; caprylic/capric/linoleic triglyceride; a synthetic medium chain triglyceride having a C₈₋₁₂ fatty acid chain; propylene glycol dicaprylate/caprate; linoleic acid ethyl ester; a cholesteryl fatty acid ester, a C₁₂₋₁₈ fatty acid monoglyceride, a C₁₂₋₁₈ fatty acid diglyceride, and a C₁₂₋₁₈ fatty acid triglyceride prepared from soybean oil, almond oil, sunflower oil, olive oil, and corn oil with glycerol; a pharmaceutically acceptable monohydric alcohol; a pharmaceutically acceptable alkanol; a pharmaceutically acceptable dihydric alcohol; a pharmaceutically acceptable aromatic ester; benzyl benzoate; diethyl phthalate; propyl gallate; triacetin; diacetin; monoacetin; triethyl citrate; a pharmaceutically suitable hydrophobic organic solvent; and a hydrofluorocarbon in the liquid state at ambient temperature and pressure.

32. (Amended) The process of claim 30 where at least one surfactant component is selected from the group consisting of a natural or synthetic amphiphilic agent; a phospholipid; a nonionic surfactant; a polyoxyethylene fatty alcohol ether; a sorbitan fatty acid ester; a polyoxyethylene sorbitan fatty acid ester; glycerol triacetate; a polyethylene glycol; cetyl alcohol; cetostearyl alcohol; stearyl alcohol; a poloxamer; a polaxamine; a polyoxethylene castor oil derivative; vitamin E; D-alpha-tocopheryl polyethylene glycol 1000 succinate; vitamin E TPGS; a PEG glyceryl fatty acid ester; PEG-8 glyceryl caprylate/caprate; PEG-4 glyceryl caprylate/caprate; PEG-32 glyceryl laurate; PEG-6 glyceryl mono oleate; PEG-6 glyceryl linoleate; a propylene glycol mono fatty acid ester; a propylene glycol di-fatty acid ester; propylene glycol laurate; propylene glycol caprylate/caprate; diethylene glycol monoethyl ether; transcitol; a monoglyceride; an acetylated monoglyceride; glycerol monooleate; glycerol monostearate; a mono-acetylated monoglyceride; a di-acetylated monoglyceride; monoacetin; diacetin; an anionic surfactant; a fatty acid salt; a bile salt; potassium laurate; triethanolamine stearate; sodium lauryl sulfate; an alkyl polyoxyethylene sulfate; sodium alginate; dioctyl sodium sulfosuccinate; sodium carboxymethylcellulose; calcium carboxymethylcellulose; a cationic surfactant; a pharmaceutically acceptable quaternary ammonium compound; benzalkonium chloride; cetyltrimethylammonium

24 bromide; lauryldimethylbenzylammonium chloride; polyethylene glycol; PEG 1000; PEG 1500; and PEG 3400.

36. (Amended) The process of claim 30, wherein the biologically active substance is selected from the group consisting of nifedipine, ursodiol, budesonide, peclitaxel, a derivative of peclitaxel, camptothecin, a derivative of camptothecin, piroxicam, itraconazole, acyclovir, a derivative of acyclovir, cyclosporine, and insulin.

37. (Amended) The process of claim 30, wherein the fluid aqueous medium is selected from the group consisting of water, buffered water, phosphate buffered water, phosphate buffered saline, citrate buffered water, acetate buffered water, water buffered with pharmaceutically acceptable pH controlling agents, water containing salts, water containing sodium chloride, water containing pharmaceutically acceptable salts, water containing soluble agents for lyoprotection, water containing soluble agents for cryoprotection, water containing dextrose, water containing mannitol, water containing trehalose, water containing sucrose, water containing sorbitol, water containing polyhydroxy-containing compounds, and a mixture thereof.
